Central perimetric sensitivity estimates are directly influenced by the fixation target

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Abstract

Purpose

Perimetry is increasingly being used to measure sensitivity at central visual field locations. For many tasks, the central (0°, 0°) location is functionally the most important, however threshold estimates at this location may be affected by masking by the nearby spatial structure of the fixation target. We investigated this effect.

Methods

First we retrospectively analysed microperimetry (MAIA-2, CenterVue, Padova, Italy) data from 60 healthy subjects, tested on a custom grid with 1° central spacing. We compared sensitivity at (0°, 0°) to the mean sensitivity at the 8 adjacent locations. We then prospectively tested 15 further healthy subjects on the same instrument using a cross-shaped test pattern with 1° spacing. Testing was carried out with and without the central fixation target, and sensitivity estimates at (0°, 0°) were compared. We also compared sensitivity at (0°, 0°) to the mean of the adjacent 4 locations in each condition. Three subjects undertook 10 repeated tests with the fixation target in place to assess within-subject variability of the effect.

Results

In the retrospective analysis, central sensitivity was median 2.8dB lower (95% range 0.1 to 8.8dB lower, $p<0.0001$) than the mean of the adjacent locations. In the prospective study, central sensitivity was median 2.0dB lower with the fixation target vs. without (95% range 0.4 to 4.7dB lower, $p=0.0011$). With the fixation target in place central sensitivity was median 2.5dB lower than mean sensitivity of adjacent locations (95% range 0.8 to 4.2dB lower, $p=0.0007$), whilst without the fixation target there was no difference (mean 0.4dB lower, SD 0.9dB, $p=0.15$). These differences could not be explained by reduced fixation stability. Mean within subject standard deviation in the difference between central and adjacent locations' sensitivity was 1.84dB for the repeated tests.

Conclusions

Perimetric sensitivity estimates from the central (0°, 0°) location are, on-average, reduced by 2 to 3dB, corresponding to a 60-100% increase in stimulus luminance at threshold. This effect can be explained by masking by the nearby fixation target. The considerable within- and between-subject variability in magnitude, and the unknown effects of disease may hamper attempts to compensate threshold estimates for this effect. Clinicians should interpret central perimetric sensitivity estimates with caution, especially in patients with reduced sensitivity due to disease.

Introduction

Though perimetry is commonly associated with non-central vision, perimetric tests of foveal and parafoveal vision have been in common use for some time. With the recently increased interest in measurement of central vision in both retinal disease and glaucoma (for reviews see Hood et al[1] and Rohrschneider et al[2]), central perimetric tests like the 10-2 program of the Humphrey Field Analyzers (Carl Zeiss Meditec, Jena, Germany, http://www.zeiss.com) and those performed by microperimeters such as the MAIA-2 (CenterVue, Padova, Italy, http://www.centervue.com) and MP-1 and MP-3 (Nidek, Japan, http://www.nidek-intl.com) are seeing increasing clinical use.

Many central perimetric tests (e.g. 10-2) do not include a test location at the central location (0°, 0°), in part due to the use of a fixation target that occupies this location. The more recent MAIA-2 microperimeter uses a central annulus fixation target that enables testing of the central location within the annulus. Indeed, the common "Expert" and "Fast" test patterns, used in the MAIA-2 include a measurement of central sensitivity. This would seem advantageous for assessment of the highest resolution region of central vision, important for tasks such as reading, face-recognition and watching television.

In static automated perimetry, sensitivity is typically measured for stimuli presented on a uniform, fixed luminance background. However, when measuring the central location with an annulus fixation target, the annulus introduces a change in the background near to the stimulus. Stimulus detection is commonly affected by the presence of surrounding structure due to visual masking mechanisms, the nature and strength of which depend on the spatial properties of the stimulus/surround[3], their location in visual space[4] and the psychophysical task being performed[5, 6]. Masking of foveal Gabor targets by surrounding flankers, for example, influences contrast detection thresholds when the flankers are separated from the target Gabor by up to approximately 2°[7]; considerably further than the distance between the fixation annulus and the central test location in the MAIA-2 microperimeter.

Masking of perimetric stimuli by surrounding texture spatially similar to the fixation annulus used in the MAIA-2 has not been previously investigated to our knowledge. Here we investigate the hypothesis that masking by the fixation annulus affects central sensitivity estimates made by the MAIA-2 microperimeter.

Methods

We conducted two investigations using the MAIA-2 microperimeter. First, data from 60 healthy observers collected for another study on a custom spatially dense grid was retrospectively reviewed, and sensitivity estimates at the central location were compared to estimates from surrounding locations. Based on previous studies of the hill of vision[8-10], we expected that the central location would have higher sensitivity than surrounding locations. Lower sensitivity could indicate an effect of the fixation annulus. Second, we prospectively tested 15 healthy observers on another custom grid, both with and without the central annulus fixation target. This second study was designed to directly test the hypothesis that central sensitivity is reduced by the presence of the fixation annulus. As an adjunct to this study we also assessed within-subject variation in central sensitivity reduction.

All studies had common inclusion criteria of visual acuity 0.2 logMAR or better in the tested eye, spherical refractive error within the range that can be compensated for by the MAIA-2 (-

15.00D to +10.00D), cylindrical refractive error less than 4.00D, age over 18 years and no known current or previous ocular disease. One eye was tested per participant, chosen randomly if both eyes met the inclusion criteria. All participants gave written informed consent to take part and for their anonymised data to be used in future studies. Both studies were approved by a local research ethics committee. All participants undertook at least one practice test using the "4-2 Expert" strategy of the MAIA-2 before experimental data were collected. Sensitivity thresholds were estimated using the MAIA-2's standard 4-2 staircase algorithm and Goldmann III (0.43° diameter) stimuli. Any tests with fixation not classified as "stable" by the MAIA-2 software were discarded and repeated.

Retrospective study

Data collected for another study were retrospectively reviewed. Healthy participants (n=60, age 19-50, median 23 years, 59 naïve to the original study purpose) undertook MAIA-2 microperimetry using 237 custom test locations placed on a square grid with 1° spacing up to 5° eccentricity and 2° spacing from 5 to 13° eccentricity (Figure 1). Participants were instructed to fixate the standard 0.76° diameter fixation annulus (Figure 1). Testing was broken into four randomly-ordered blocks in each of which an evenly-spaced subset of test locations was tested. Testing was completed over one or two study sessions lasting up to one hour, incorporating rests between tests as needed.

For the present study, we compared sensitivity at the central (0°, 0°) location to mean sensitivity at the eight immediately adjacent test locations (Figure 1).

Prospective study

Healthy participants (n=15, age 21-51, median 26 years) undertook MAIA-2 microperimetry using a custom grid with 17 locations arranged in a cross pattern centred on (0°, 0°) with 1° spacing up to a maximum of 4° eccentricity (Figure 1). This pattern was chosen to allow short test duration but with spatial uncertainty approaching that of the 4-2 "Expert" test commonly used on the MAIA-2. Both authors participated; the remaining participants were naïve to the purpose of the study.

Testing was carried out under two conditions, one with the central annulus fixation target, and one without. In the "without" condition, the large annulus target (12° diameter, Figure 1) was displayed, centred on (0°, 0°). Since it is not possible for the MAIA-2 to display only the large circle, an additional small cross was displayed at (-2°, 4°). This is the furthest available location from the centre and does not impinge on any tested locations. In the "without" condition the observers were instructed to ignore the cross and fixate as steadily as possible in the centre of the large circle. In the "with" condition observers fixated in the centre of the standard 0.76° diameter annulus as normal. Each condition was repeated twice in random order, and the results of the two repeats were averaged. Testing was completed within a single session of up to 30 minutes, incorporating rests as needed. All participants gave informed consent to take part.

To test the hypothesis that the fixation annulus alters central sensitivity estimates, we made within-subject comparisons of:

(i) Central sensitivity with vs. without the fixation annulus.

(ii) Central sensitivity vs. the mean of the four immediately adjacent locations (Figure 1) with the fixation annulus (similar to the retrospective study).

(iii) Identical to (ii) except without the fixation annulus.

We also compared sensitivity at the four immediately adjacent locations with vs. without the fixation annulus within subjects. To assess within-subject variation in central sensitivity difference from surrounding locations, three participants (ages 30-35, including both authors) undertook a further eight tests under the "with" condition (total n=10 repeats). In-between these repeated tests the participants moved away from the instrument, and the instrument was adjusted to a completely different position before re-positioning for the participant in order to simulate separate clinic visits.

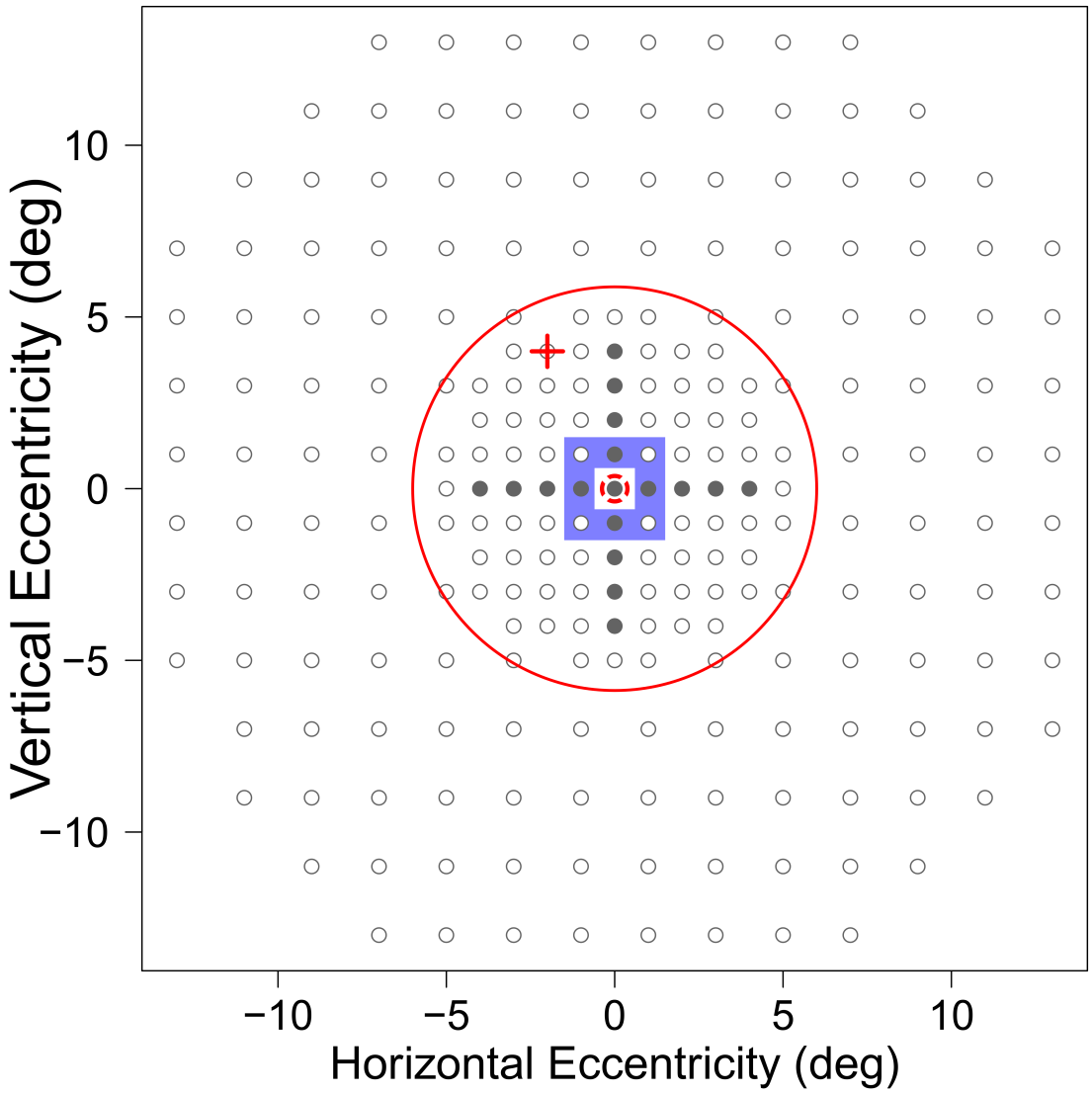

Figure 1: *Test locations used, locations compared to the central (0°, 0°) location, and the positions of the two fixation annuli. The unfilled grey circles represent the test locations used in the retrospective study. The filled grey circles represent test locations used in both studies. The smaller red annulus represents the standard fixation annulus, the larger red annulus represents the annulus used only in the "without" condition in the prospective study. The red cross at (-2,4) was present only for the "without" condition in the prospective study. Test locations shown on the shaded blue background were included in the comparisons to the central location. Stimuli and annuli are drawn to scale.*

All statistical analyses for both studies were carried out in the open-source environment, *R*[11] (version 2.15.0, https://www.r-project.org/). Comparisons were made on a within-subject basis using paired t-tests when data were normally distributed or Wilcoxon signed-rank tests

when they were not. Normality of data was assessed by Kolmogorov-Smirnov tests and visual comparison of data quantiles to normal quantiles. Statistical significance was assumed at $p<0.05$. Since we made a relatively small number of planned comparisons we did not use a correction for multiple comparisons.[12]

Results

Retrospective study

Figure 2 shows example data from one participant, including the custom pattern of test locations and those included in the comparison with the centre location.

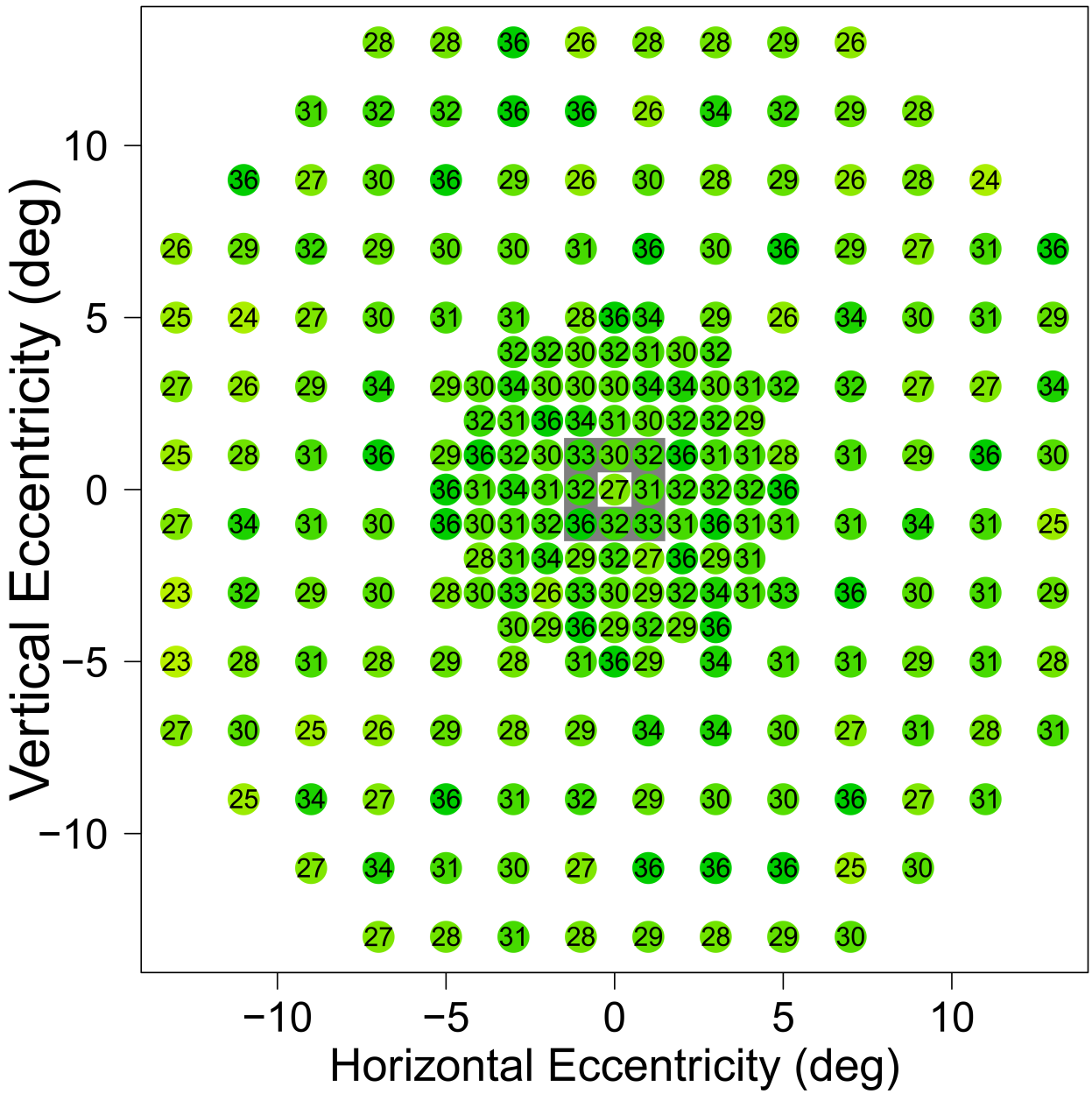

Figure 2: *Example of one participant's central visual field from the retrospective study. The custom test pattern included locations spaced on a 1° square grid up to an eccentricity of 5°, then spaced on a 2° square grid from 5 to 13° eccentricity. Sensitivity at the central location (0°, 0°) was compared to the mean of the surrounding eight locations, shown here on a gray shaded background. Sensitivity (dB) at each location is indicated. Note the reduced sensitivity at the central location.*

Contrary to what would be physiologically predicted in the absence of confounding factors, threshold sensitivity at the central location was median 2.8dB (95% range -8.8 to -0.1dB) lower than the mean of the surrounding eight locations ($p<0.0001$, Wilcoxon signed-rank test). Central sensitivity was at least 1dB lower than the mean of the surrounding locations for 54 of 60 participants (90%).

We additionally compared sensitivity at the central location to the mean sensitivity at the four closest cardinal points (shaded points within the blue box in Figure 1) and to the mean sensitivity at the four closest ordinal points ((±1°, ±1°) unshaded points within the blue box in Figure 1) since the latter are 0.41° further away from the fixation annulus. Mean sensitivity at the cardinal points was mean 0.6dB (SD 1.0dB) lower than mean sensitivity at the ordinal points (paired t-test, $t(59)=4.34$, $p<0.0001$). Sensitivity at the central location was median 3.3dB (95% range -8.4 to -0.5dB) lower than mean sensitivity at the ordinal points ($p<0.0001$, Wilcoxon signed-rank test) and was median 2.5dB (95% range -9.3 to 1.1dB) lower than mean sensitivity at the cardinal points ($p<0.0001$, Wilcoxon signed-rank test).

Prospective study

Figure 3 shows example data from one participant, including the custom pattern of test locations and those included in the comparison with the centre location.

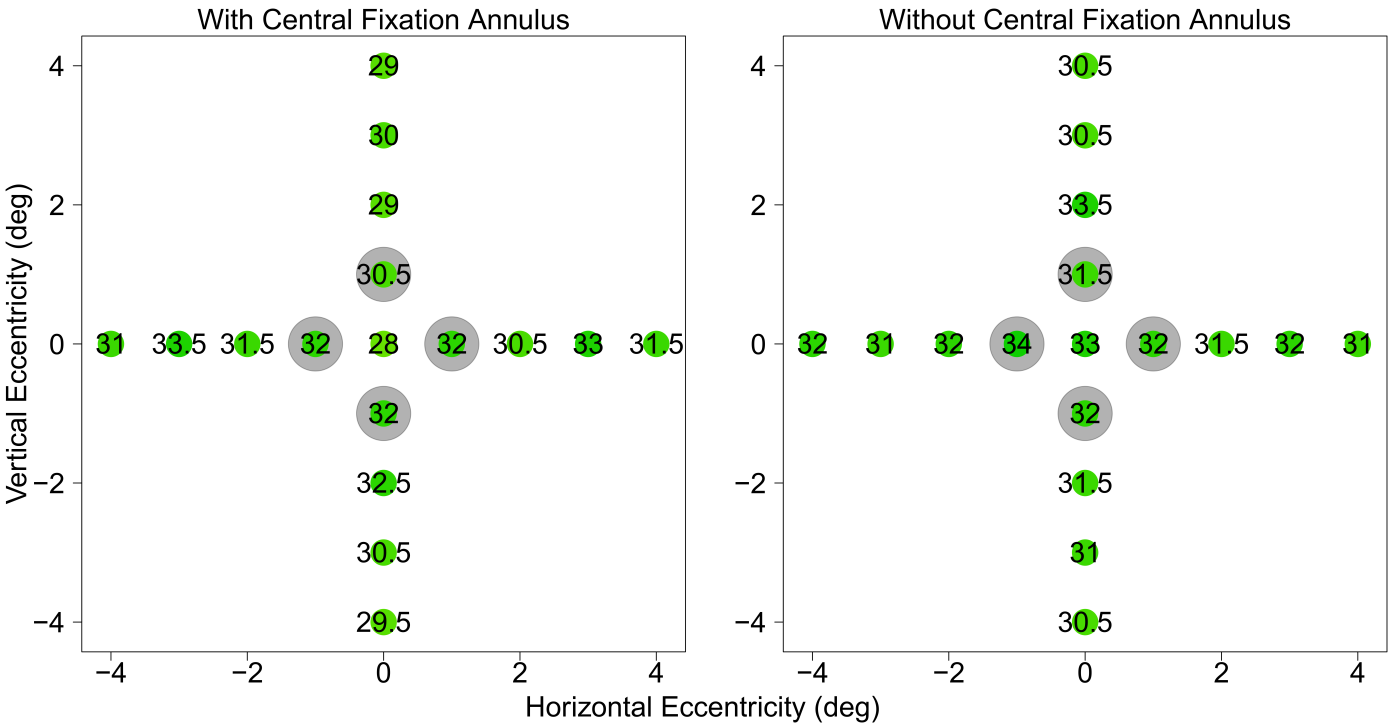

Figure 3: *Example of one participant's central visual field from the prospective study when the central fixation annulus was present (left) and absent (right). The custom test pattern included 17 locations spaced 1° apart in a cross pattern as shown. Sensitivity at the central location (0°, 0°) was compared to the mean of the surrounding four locations, shown here on a grey shaded background. Sensitivity (dB) at each location is indicated. Note that sensitivity at the central location was reduced when the fixation annulus was present (left), but not when it was absent (right).*

In our participants, fixation stability was acceptable, though reduced when the central annulus was removed. With the central annulus, median 95% bivariate contour ellipse area of fixation was 0.30 deg^2, whilst without the central annulus this increased to 2.05 deg^2 (p=0.0011, Wilcoxon signed-rank test). If unstable fixation had affected the results, we would expect the surrounding locations to have greater average sensitivity when the fixation annulus was not present due to fixation wandering to the stimulus locations. There was in fact no significant difference in mean sensitivity at surround locations under the two conditions (mean difference 0.1dB higher without the fixation annulus, standard deviation 0.8dB, paired t-test: t(14)=0.31, p=0.76).

Central sensitivity was median 2.0dB (95% range -4.7 to -0.4dB) lower when the central fixation annulus was present compared to when it was not (p=0.0011, Wilcoxon signed-rank test).

Similar to the retrospective study, when the fixation annulus was present, central sensitivity was median 2.5dB (95% range -4.2 to -0.8dB) lower than the mean of the surrounding four locations (p=0.0007, Wilcoxon signed-rank test). When the fixation annulus was not present, however, there was no clinically or statistically significant difference in sensitivity between the central and surrounding four locations (mean difference central location 0.4dB lower, standard deviation 0.9dB, paired t-test: t(14)=1.51, p=0.15).

For the three subjects who conducted ten repeats with the standard fixation annulus present, within-subject standard deviation in difference between sensitivity estimates at the central location and the four adjacent locations was 1.84dB.

Discussion

The presence of the standard central fixation annulus in the MAIA-2 microperimeter reduced estimates of healthy observers' central sensitivity by 2-3dB on average. This effect was not present when testing was conducted without the fixation annulus. This is a large and potentially clinically significant reduction in sensitivity, being equivalent to a 60-100% increase in stimulus luminance at threshold.

The effect of the fixation annulus on detection thresholds observed in this study can be described as masking by the fixation annulus. Masking effects of nearby or surrounding texture on the detection of stimuli are ubiquitous in human vision, and their nature depends on a variety of factors including location in visual space[4], relative spatial properties of the stimulus and surround[3] and the psychophysical task being performed[5, 6]. Key examples include overlay masking, in which non-target objects overlay the receptive fields involved in detection of the target stimulus, and surround suppression in which surrounding objects stimulate receptive fields not directly involved in detection of the target stimulus yet still impair stimulus detection by lateral inhibitory processes[4]. It is therefore likely that the present observation can be explained by similar mechanisms to those already reported in laboratory psychophysics and animal models, though an in-depth exploration of these possibilities is beyond the scope of this study.

It may be tempting to simply employ an empirical correction factor to the central location, such as adding 2-3dB to the estimated sensitivity, for clinical purposes. This may be a useful

first pass in reducing bias in central threshold estimates on average and for healthy subjects. However, such a correction must be applied whilst bearing in mind its limitations. First, such a simple correction assumes that the visual system's response to contrast is linear. Whilst this may be approximately true over a narrow range of contrasts, it is demonstrably not true over wider ranges, particularly at low luminance[13]. This may be particularly important for individuals with sensitivity loss due to disease, where this relationship may be less linear and contrast gain may also be altered[14, 15]. Second, the magnitude of the reduction is empirically highly variable both within- and between-subjects. Some of the masking effects mentioned above change with age[16-18], and vary considerably between individuals[19]. This makes a simple correction for the average reduction unlikely to be accurate for any one test. It is also worth emphasising that the effect observed in this study is likely to hamper the monitoring of progressive sensitivity loss at this location, as the effects of the annulus on sensitivity estimates may not be constant or linear with sensitivity loss due to possible concurrent changes in contrast gain and masking mechanisms.

There are at least three reasons for the high variability in the sensitivity reduction at the central location. Measurement variability and between-individual variability in contrast gain and masking mechanisms (as mentioned above) will surely contribute to this variation, but the third, possibly major, contributor to the variability in our data is parallax displacement of the test stimulus relative to the annulus depending on the precise alignment of the eye relative to the instrument. We note that with the MAIA-2, even small lateral shifts of head position can cause significant parallax displacement, in some cases causing the central stimulus to overlay a portion of the fixation annulus. Clearly, such changes in the distance between the stimulus and the fixation annulus are likely to affect the sensitivity reduction induced by the annulus. To this end, it may be possible to reduce these effects considerably by using an alternative fixation target that does not affect the immediate surround of any stimulus as much. One possibility would be a broken cross target, though this remains to be tested. An alternative might be to have a changing fixation target, depending on the location under test, though this would have the potentially negative affect of providing spatial cueing to the test subject and may also affect fixation stability.

Though the MAIA-2 and similar microperimeters employ a number of additional technologies (e.g. eye-tracking, fundus imaging) beyond that of conventional perimeters, none of these impact upon our findings. Therefore, although we used a MAIA-2 microperimeter in this study, we expect that our results will generalise to other perimeters or experimental procedures that use a nearby fixation target to enable testing of the central location.

The comparison of sensitivity at the central location to that of adjacent locations is limited by the assumption that true sensitivity at the central location is at least equal to the adjacent locations. In reality, true central sensitivity is likely to be higher than at adjacent locations[8-10], so it is likely that the "true" reduction in measured sensitivity is actually slightly greater than reported. Nevertheless, our findings appear robust across a number of participants when tested both prospectively and retrospectively, and the reduction in sensitivity is also apparent when comparing across tests carried out with and without the fixation target in place. When testing without the central fixation target, fixation was worse than with the target in place (though still within acceptable limits). However, this did not affect sensitivity at surrounding locations, and would only be expected to reduce sensitivity at the central location, thereby reducing the difference between the "with" and "without" fixation target conditions.

The reduction in measured sensitivity at the central (0°, 0°) location is a clinically relevant problem that those using central perimetry should be aware of. Central sensitivity estimates

are likely to be significantly reduced by the presence of the annulus. Whilst adjustment of sensitivity estimates by 2-3dB will reduce this bias in healthy subjects, this correction may not be accurate in patients with reduced sensitivity due to disease. In certain perimeters, estimates of central sensitivity may also be highly variable unless great care is taken to align the subject carefully such that the central test location is centred in the annulus, and to maintain this position throughout the test. Central sensitivity estimates should therefore be interpreted with caution when assessing foveal damage or disease progression.

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